

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 15 MAY 2006

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Applicant's or agent's file reference MMV/PB60521	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2004/013076	International filing date (day/month/year) 17.11.2004	Priority date (day/month/year) 19.11.2003	
International Patent Classification (IPC) or national classification and IPC INV. A61K31/513 A61K31/5025 A61K31/44 A61P25/18			
Applicant GLAXO GROUP LIMITED			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 11.10.2005		Date of completion of this report 12.05.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Skjöldebrand, C Telephone No. +49 89 2399-	



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/013076

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-48 as originally filed

Claims, Numbers

1-33 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 2,3,17-33

because:

☒ the said international application, or the said claims Nos. 17-33 (I.A. only) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 2,3

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1,4-33 .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1, 4-33
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1, 4-33
Industrial applicability (IA)	Yes: Claims	1, 4-16
	No: Claims	17-33

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 17-33 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

The current application is directed to the problem of providing alternative pharmaceutical agents for treating schizophrenic disorders. The proposed solution is the use of COX-2 inhibitors of formulae (I)-(III), as in claims 1-3.

The concept of using inhibitors of COX-2 in the treatment of schizophrenic disorders is however known, cf. D1. As the COX-2 inhibitors of formulae (I)-(III) do not have a significant structural element in common, no novel and inventive concept exists so as to unify these claims.

The application does not meet the requirements of unity of invention as defined in Rules 13.1 and 13.2 PCT.

For the above reasons, only a partial search was performed by the ISA, cf. also separate sheet of the ISR. The following discussion therefore deals with the first invention listed in the ISR, namely:

Claims 1, 4-33 Compounds of formula (I) for use in the treatment of schizophrenic disorders.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: US 2003/130334 A1 (MULLER NORBERT [DE]) 10 July 2003 (2003-07-10)
- D2: WO 02/096885 A (GLAXO GROUP LIMITED; NAYLOR, ALAN; PAYNE, JEREMY, JOHN; PEGG, NEIL, AN) 5 December 2002 (2002-12-05)
- D3: RIEDEL M ET AL: "Rational and efficacy of COX-2-inhibitors as adjunctive therapy in schizophrenia." EUROPEAN NEUROPSYCHOPHARMACOLOGY, vol. 13, no.

Supplement 4, September 2003 (2003-09), page S96, XP001205337 & 16TH CONGRESS OF THE EUROPEAN COLLEGE OF NEUROPSYCHOPHARMACOLOGY; PRAGUE, CZECH REPUBLIC; SEPTEMBER 20-24, 2003 ISSN: 0924-977X

D4: MUELLER N ET AL: "BENEFICIAL ANTIPSYCHOTIC EFFECTS OF CELECOXIB ADD-ON THERAPY COMPARED TO RISPERIDONE ALONE IN SCHIZOPHRENIA" AMERICAN JOURNAL OF PSYCHIATRY, AMERICAN PSYCHIATRIC ASSOCIATION, WASHINGTON, DC, US, vol. 159, no. 6, June 2002 (2002-06), pages 1029-1034, XP008015002 ISSN: 0002-953X

Please refer to the pages, lines etc. of the cited documents as indicated in the International Preliminary Search Report.

Inventive Step - Article 33(3) PCT

The applicant discloses test-results demonstrating a selective inhibition of COX-2 for the substances in question, a fact that was known from D2. There appears to be no substantiated evidence of the claimed effect against schizophrenic disorders, merely an experimental protocol for a patient-study. It follows that the extrapolation from COX-2 inhibition to an antischizophrenic effect could have been done also from D2. D2 taken alone is therefore considered to anticipate the subject-matter of independent claims 1, 12 and 17.

This is especially valid since D1 and D3-D5 disclose the use of various COX-2 inhibitors in the treatment of schizophrenic disorders. The combination with risperidone is also foreseen (cf. D1, D3, D4).

An inventive step can therefore not be acknowledged for the subject-matter of claims 1 and 4-33.

Industrial Applicability - Article 33(4) PCT

For the assessment of the present claims 1 and 4-33 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known com-

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pound for first use in medical treatment and the use of such a compound for the
manufacture of a medicament for a new medical treatment.